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PROPOSAL TITLE:	METABOLISM AND DOSIMETRY OF PLUTONIUM INDUSTRIAL COMPOUNDS PROJECT 2.1 ESTABLISHED PER AGREEMENT BETWEEN THE GOVERNMENTS OF THE UNITED STATES OF AMERICA AND THE RUSSIAN FEDERATION
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ABSTRACT

Since March 1, 1995, scientists of the Dosimetry Registry of the Mayak Industrial Association (DRMIA) and the United States Transuranium and Uranium Registries (USTUR) have been involved in a collaborative one-year study to compare methods used by the two Registries and the data collected by those methods and to compare combined data to existing actinide biokinetic models. Progress of the program was presented in two progress reports, one submitted in October 1995 and another submitted in January 1996. During the year, an number of specific objectives for further collaborative study were identified and approaches toward achievement of those objectives were formulated. This is a proposal for a three-year extension of the collaborative research program.

Research areas included in the proposed program include:

- intercomparison of radiochemical and other analytical methods used by the two Registries through sample exchanges and procurement by the DRMIA of modern instrumentation and high purity reagents, including tracer radionuclides, not currently available in the Russian Federation;
- establishment of database formats for each proposed task in which combined data of both Registries are to be used;
- coordination of tissue sampling methods for future autopsies to be performed by each Registry to facilitate and improve data comparisons;
- analysis of physico-chemical characteristics of workplace aerosols currently being measured by the DRMIA and previously measured by U. S. nuclear facilities at which USTUR donors were employed;
- analysis of combined data from both Registries to establish transfer coefficients of actinide elements between lungs, lymph nodes, and other body organs in healthy individuals and those with health impariments, specifically liver diseases;
- evaluation of combined data from both Registries to establish relationships between actinide contents of the lungs and other body organs at autopsy and long-term urinary actinide excretion rates;
- enhancement of DRMIA in vivo counter capabilities with intercomparisons with counters of other laboratories using U. S. phantoms and procurement of more sensitive detection instrumentation for the DRMIA;
- translation into English and publication of previously classified Russian documents containing actinide metabolism and dosimetry information for sharing with the world scientific community; and

- exploration of the feasibility of performing cytogenetic studies to correlate chromosomal abnormalities with conventional dosimetry and bioassay evaluations.

The proposed program has obvious direct applicability to validation and improvement of radiation protection standards for actinides and to the better understanding of the biokinetics and dosimetry of the actinides in man. The results of this research will also be in direct support of epidemiologic and radiation effects studies conducted in conjunction with this dosimetry program.

1. BACKGROUND

Scientists of the Dosimetry Registry of the Mayak Industrial Association (DRMIA) and the United States Transuranium and Uranium Registries (USTUR) have been involved in a collaborative research program since March 1995. During this time, they have been comparing methods used by both Registries to collect data and have begun to investigate the comparability and compatibility of data collected to date. This is a proposal for continued collaborative research between the two Registries for an additional three-year period.

The primary potential health hazard to personnel working with actinides in nuclear facilities is the intake of plutonium and, to a lesser extent, americium and other actinides. Since 1968, the USTUR has been studying the biokinetics, dosimetry, toxicity, and other possible biological effects in humans of the actinide elements utilizing radiochemical analysis of human organ and tissue samples collected at autopsy from volunteer donors with documented exposures to actinides. An analogous research program, the DRMIA, has been conducted by the First Branch of the Biophysics Institute of the Russian Federation since the early 1970's. This Russian Registry has conducted in vivo screening of Mayak workers by whole body counting for ^{241}Am, dosimetry by analysis of excreta samples for plutonium and americium, and radiochemical analysis of post-mortem human tissue samples collected at autopsy.

The DRMIA and USTUR were formed with similar objectives, to examine the metabolism, dosimetry, and possible biological effects of actinide elements in occupationally-exposed humans. Achievements of both Registries are reflected by numerous publications in the open literature. Distributions of actinides in the human body were the subjects of numerous reports by American scientists, including recent publications by McInroy, et al. (1989), Kathren, et al. (1993), Filipy, et al. (1994), Filipy and Kathren (1996), and

Russian scientists, Khokhryakov et al. (1995a), Suslova and Khokhryakov (1985), Khokhryakov, et al. (1989), and Suslova et al. (1993). Comparisons of in vivo estimates of body burdens with post-mortem analysis of tissues were reported by Kathren et al. (1987), Kathren and McInroy (1991), and Khokhryakov, et al. (1994). Suggestions for improvements in biokinetic models were made by Kathren and McInroy (1992), Kathren (1994), Khokhryakov et al. (1975) and risks associated with actinide body burdens were the subject of a report by Khokhryakov and Romanov (1994), Khokhryakov et al. (1995b), Hohryakov et al. (1994), and Hunacek and Kathren (1995).

The current biokinetic models for plutonium and americium, which serve as the basis for radiation protection standards, are largely based on experimental animal data and data from short-term human studies including in vivo followups of persons with acute accidental exposures (ICRP-30 1979; ICRP-48 1986; ICRP-66 1994; ICRP-67 1994). Integration and metanalysis of data collected over several years by the Russian DRMIA and the American USTUR is expected to enable scientists to more effectively correlate actinide metabolism with exposure times and to verify or suggest modifications of biokinetic models for long-time, chronic exposures. This would provide an improved basis for establishment of radiation protection standards and evaluation of occupational exposures as well as improve actinide dosimetry, which could then be correlated with possible radiobiological effects. The dosimetric information resulting from this work will be in direct support of Projects 2.2 and 2.3 which are concerned with risk estimation for stochastic (carcinogenic) and deterministic consequences, respectively, of occupational exposure to actinides. The information will also be useful to Projects 1.1 and 1.2 which are concerned with dose reconstruction and stochastic effects in the general population of the Eastern Ural region.

There are a number of advantages from a collaborative research effort between USTUR and DRMIA scientists with much to be gained. The USTUR and the DRMIA have post mortem data from more than 250 and more than 750 deceased registrants, respectively, although specific data for the various individual cases differ in many instances, limiting comparisons. Collaboration would increase the number of cases available for study by a factor of four for already deceased registrants relative to the number of USTUR cases. In addition to enhanced statistical power for data analysis, data comparisons of the two Registries might also enable certain otherwise unrealizable goals such as dose-dependence or dose-independence of biokinetic parameters to be acheived. Actinide deposition levels in past DRMIA cases were much higher than those of the USTUR cases; estimated actinide body burdens of USTUR cases at the time of death generally range from 40 Bq to 300 Bq with a few cases falling outside this range. Those

measured by the DRMIA range between approximately 40 Bq to 175 kBq. This is reflected in the comparison of liver concentrations in Figure 1. Combination of data from the two registries will also result in a greater heterogenicity of the worker population; the DRMIA have data from many female workers while the USTUR database contains data from only a few females.

2. PRELIMINARY STUDIES

The Project 2.1 feasibility study revealed a number of similarities and some basic differences in the scopes of operation and data collection methods of the two Registries (Suslova et al. 1996) including the following:

- the USTUR cases are derived from a number of work sites with differing operational practices as well as dosimetry, bioassay, and medical practices; the DRMIA cases all worked at a single site and hence are likely more homogeneous in terms of exposure histories and dosimetry;
- autopsies on DRMIA cases have been performed by a single group of pathologists, as compared with the USTUR which relies on pathologists available at the location and time of registrant death;
- the USTUR has received and analyzed several whole-body donations which have provided more complete data regarding distribution of the actinide elements within the body;
- actinide levels in tissue samples collected by the DRMIA were generally higher than those of the USTUR with median levels of DRMIA cases about two orders of magnitude greater than those of USTUR cases;
- tissues collected by the DRMIA have all been analyzed on site by a single laboratory over the years while USTUR tissues have been analyzed by four separate laboratories, with intercomparisons available, and;
- radiochemical analytical techniques differ between the two Registries; the DRMIA utilizes co-precipitation techniques and direct scintillation counting while the USTUR routinely uses radiotracers with alpha spectrometry with state-of-the-art counting equipment.

A trial combination of DRMIA and USTUR data was used to investigate the comparability and compatibility of data collected by both Registries. For each Registry, measured postmortem plutonium concentrations in the skeleton and liver and the times between exposure to plutonium and death of each case (residence times) were evaluated and compared. Liver and skeleton were used because these are organs of preferential deposition of actinide elements in the human body.

Figure 1 shows frequency distributions of the cases from each Registry with respect to liver concentrations of plutonium. For both Registries, the ranges of concentrations were log-normally distributed. The DRMIA cases had significantly higher liver concentrations with a median concentration of 407 Bq/kg compared with a USTUR median concentration of 1.7 Bq/kg. More than 90% of the DRMIA cases had liver concentrations greater than those of USTUR cases, hence there was little overlap in the distributions.

The differences between minimum and maximum concentrations was also of interest. USTUR liver concentrations ranged from 10^{-2} to 10^{3} Bq/kg while the concentrations reported by the DRMIA were much more tightly grouped, ranging from 10^{2} to 10^{4} Bq/kg; the limited range and the apparent truncation at the low end of the DRMIA data may be a result of case selection. However, the reasons for the differences in the concentrations observed in the cases of the two Registries need to be more fully determined and documented. At this time, such factors as systematic error, reporting differences, and case selection criteris need further evaluation.

Plots of skeletal:liver plutonium concentration ratios versus residence times are shown in Figure 2 for the combined data of both Registries. Ratios for USTUR range over two orders of magnitude, from approximately 0.02 to 2.0. DRMIA ratios were much less variable, ranging between approximately 0.07 and 0.7, or only over one order of magnitude. Despite the difference in spread and uncertainties in concentration ratios, the data from both laboratories imply that the skeleton:liver concentration ratios remain essentially the same regardless of the time between exposure and death (residence time). Thus there is no apparent or significant practical difference between the clearance half-times of plutonium from the skeleton and liver. These results are compared with the model predictions for plutonium recently put forth by the ICRP-67 (1994). While the comparison suggests that the ICRP model slightly overestimates skeletal content, underestimates liver content, or both in that the majority of observed ratios fall below the ICRP-predicted ratios, because of the variability in the observed data, the difference between the ICRP model and the regression line through the observed ratios is not statistically significant. It is important to continue these data analyses to determine if this is meaningful.

Similar observations were made when skeleton:liver americium concentrations ratios were compared with those predicted by the ICRP model. The majority of observed ratios were below the model-predicted line and, as with plutonium, no differences between skeletal and liver retention half-times were noted at residence times greater than 20 years. As with plutonium, the variability in the observed data precludes a statistical significance in the difference between the ICRP model and the regression line through the observed data.

Skeleton:liver concentration ratios were evaluated as a function of liver concentration which was considered to reflect the body burden (Figure 3). Skeleton:liver concentration ratios in cases of the two Registries appear constant regardless of the differences in plutonium body burdens of the cases.

The DRMIA and the USTUR databases contain essentially the same kinds of data. The DRMIA database was constructed with the software, FOX-PRO while the USTUR was constructed with the software PARADOX. Both are capable of importing and exporting files from other database software as well as by the use of text files. In discussions between personnel of both Registries, it was not considered necessary or desirable to try to combine both complete databases into one. Rather, it was decided that specific kinds of data would be necessary for completion of many of the objectives listed below and a database format would be designed to receive specific data for each task. This would enable each Registry to independently query its respective databases for those data, verify the data, and transfer it to a common database electronically, thus precluding the possibility of transcription errors. The common database would then be available to scientists of both organizations.

3. SPECIFIC AIMS

The following objectives represent the major tasks to be accomplished during continued collaboration between personnel of the DRMIA and the USTUR. It is anticipated that smaller ancillary tasks related to these tasks will become apparent during work on the major objectives. Much behind-the-scenes work will be necessary for both Registries such as compilation of relevant data, formatting the data for common use, and verification of data as they are transferred to a common database. Figure 4 shows the anticipated schedule of initiation and completion of each task.

The major specific tasks are to:

A. intercompare radiochemical analytical methods for actinides currently in use by both Registries with a series of performance evaluations;

B. establish a common database format that can be used by both Registries for completion of the the tasks listed below;

C. relate tissue sampling methods used by the two Registries including specific tissues and organs sampled, mass of the

sample, and specific structures to be included in a sample, thus improving and making more exact data comparisons;

D. coordinate radiochemical analytical methods used by both Registries to determine actinide contents of tissue samples, including ashing methods, actinide separation techniques, spectroscopy methods, and data recording;

E. characterize workplace aerosols at the Mayak facility and American facilities. This will be accomplished by reviews of existing records and by measuring physico-chemical properties such as particle size distribution and in vitro solubility for the purpose of more accurately predicting their initial deposition and solubility in the lungs of workers;

F. establish transfer coefficients, based on the systemic:lung:lymph node activity ratios measured by both Registries, that describe the transfer of various plutonium and americium compounds from the lungs to the blood and compare the coefficients with those predicted by the new ICRP-66 (1994) models for the purpose of testing the model directly with human, long-term exposure data;

G. determine the relationships between actinide concentrations of organs of the body and between individual organs and total body burdens in healthy individuals as well as in those with health impairment, specifically those with liver diseases;

H. test the relationships between actinide contents of the lungs and body organs at autopsy and the long-term, temporal pattern of urinary excretion predicted by the current ICRP metabolic models for plutonium and americium (ICRP-67 1994) and to compare actinide metabolism and long-term urinary excretion of the actinides in healthy individuals with that in health-impaired individuals, specifically in those with liver diseases;

I. enhance the sensitivity of the in vivo counter used by the DRMIA and perform calibrations and intercomparisons with other, similar facilities so that it is a more useful tool for characterizing the intake and retention of actinide elements;

J. translate previously classified Russian documents into English for submission to peer-reviewed journals or for pulication as topical reports, as appropriate;

K. tissue autoradiography to determine the spatial and temporal distributions of plutonium in tissue samples, primarily the lungs, lymph nodes, and liver, and;

L. initiate biomarker assays including the fluorescence in-situ hybridization (FISH) assay and glycophorin A (GLA) analysis to detect radiation-induced chromosomal translocations in peripheral blood lymphocytes and erythrocytic stem cells, respectively.

4. RESEARCH DESIGN AND METHODS

Although much progress has been made toward comparison of the data collected thus far by the two Registries, there is still much detailed comparison to be accomplished. For that reason, the descriptions of many tasks to be performed are necessarily general and represent scientific approaches rather than detailed research designs. It is also noted that the list of tasks is quite ambitious and it may not be possible to conclusively complete some of them within the time frame proposed.

Task A

The first progress report of this collaborative research program (Suslova et al. 1995) contained a detailed comparison of the methods by which the DRMIA and the USTUR collected the data that they now have in each of their respective databases. One of the primary differences between the operations of the two Registries relates to the radiochemical analytical methods and instrumentation. Current procedures differ significantly. Intercomparisons of the methods and equipment is necessary to assure comparability and compatibility of existing data or to quantify any consistent differences in analytical results. Ideally, the first step would be to exchange stainless steel disks containing electrodeposited samples; however, differences in the configurations of counting instruments used by the two laboratories preclude such an exchange. An initial exchange of acid-dissolved tissue samples is proposed to compare electrodeposition and counting methods and it is planned as one of the first tasks to be performed. The initial intercomparisons will be evaluated and the intercomparison program expanded to include analyses of U. S. National Institute of Standards and Technology (NIST) reference materials as the DRMIA laboratories methods and equipment are updated and as new methods are developed by the USTUR laboratories (Task D). The first phase of this work (exchange of acid-dissolved samples) is scheduled for

completion by October 1, 1997; however, other performance evaluations will be continued, as needed, for the duration of the program.

Task B

The DRMIA and the USTUR both have computerized databases containing exposure, dosimetry, and medical data as well as radiochemical analytical data from autopsy tissue samples. The purpose of this task is to design a database format in which only data relevant to the collaborative research projects listed below can be stored and can be available to researchers of both Registries in a compatible format. No personal identifiers will be exchanged between laboratories. The initial part of this task is expected to be completed by June 1, 1997 with further modifications as necessary throughout the remainder of the project.

Task C

The soft tissue sampling methods in use by the two Registries are already quite similar. The main difference is in the kinds of bone samples collected. The USTUR routinely collects ribs, clavicles, sternums, patellae, and vertebral wedges while the DRMIA collects ribs, a vertebral wedge, samples from the occipital and temporal bones of the skull, a sample of ilium, and the distal end of a femur. For both Registries, the relationship of actinide concentration and total content of specific tissues and organs will be evaluated to determine correlations with total system burdens, or with depot sites. In addition, the results of this evaluation will be used to assess the validity and overall utility of the tissue sampling protocols used by each Registry, and to develop indicated refinements to those protocols. Specific tissues to be considered include lymph nodes, bone marrow samples, structures of the circulatory system and all bone samples. This will be the first major task to be completed with an anticipated completion date of February 1, 1997.

Task D

The USTUR utilizes state-of-the-art radiochemical analytical techniques and associated instrumentation, including multidetector alpha spectrometry instrumentation. Such instrumentation has not been available to the DRMIA. Means of acquisition of comparable equipment for the DRMIA laboratories will be explored. DRMIA equipment in current use has been adequate in the past because of the relatively high actinide activity in the samples analyzed. As time progresses, however, the alpha spectrometry equipment, routinely

used by the DRMIA for tissue and urine samples, may not be adequate because the samples from more recent cases contain lower concentrations of actinides and because many of their registrants have worked with ^{238}Pu in the Mayak isotope production facility. The DRMIA also has great need for high purity ^{242}Pu and ^{243}Am tracers which are not available in the Russian Federation and methods of obtaining those tracers will be explored.

As part of its primary program, the USTUR personnel are investigating new methods for chemical separation of actinide elements such as the potential use of "Tru-Spec" ion exchange columns, which would be more efficient and less time consuming than current methods. After reliable procedures with these methods have been established at USTUR laboratories, the possibility of their use by the DRMIA laboratories will be investigated. This task will require much time and attention and completion is not anticipated before the end of the proposed work period, September 30, 1999.

Task E

Scientists at the DRMIA have developed a dialysis method for measurement of in vitro solubility of alpha-active aerosols (Khokhryakov 1995). They have also acquired a cascade impactor for measurement of aerosol particle size distribution in the workplace. Physico-chemical characterization of workplace aerosols is an integral part of determining the deposition of inhaled particles in the lung. The degree to which aerosol properties affect absorption of actinides from the lung will be determined by comparing systemic and lung contents of actinides in cases exposed to aerosols of different physico-chemical properties.

Data on the physico-chemical characteristics of actinide aerosols collected by the DRMIA, together with those collected by the USTUR as part of registrant exposure histories, with estimates of the temporal patterns of exposure for each registrant, will be used with the current ICRP models of the respiratory tract and actinide metabolism to predict the lung, lymph node, and organ contents and doses expected at the time of autopsy. The distribution of predicted values will be compared with the data from both Registries. This task is scheduled for completion by June 1, 1999.

Task F

DRMIA scientists have studied absorption of various plutonium and americium compounds from the lung into systemic circulation after inhalation intake for many years (Khokhryakov 1995) and such studies were also the subject of a report by USTUR scientists (Kathren et al. 1993). The

most complete sets of data for individual registrants of both Registries, which include reliable information on temporal exposure patterns and/or temporal urinary excretion in addition to lung and body organ contents at autopsy will be selected for detailed dosimetric analysis. In each case, the current ICRP models of the respiratory tract and systemic metabolism will be exercised to apply the measured radiochemical data to derive an estimate of the effective rate of absorption of actinide elements from the lungs, and the resulting total organ doses as a function of time since the start of exposure. This procedure will identify any major underlying deficiencies in the ICRP models by means of any consistently observed failure to match the observed ratios of lung:body organ contents. The anticipated completion date for this task is October 1, 1989.

Task G

Determination of actinide biokinetics in the human body is an ongoing effort within both Registries. Briefly, the work involves the use of ratios between actinide concentrations in small organs such as the spleen and testes and those in the larger organs that are the major deposition sites in the body (ie: liver and skeleton). The tissue:liver (for example) concentration ratios are regressed against the residence time (the time between exposure or presumed exposure and death). The regressions are used as indicators of differences between retention half-times of the tissue in question and the liver and the y-intercept of each regression indicates relative initial fractional deposition in the tissue and liver (Filipy and Kathren 1996). With that information from several tissues and organs of the bodies of routine autopsy cases and whole body donations to the USTUR, much can be learned about the retention half-times and initial distribution of actinides throughout the body. This information will be used to indicate the degree of variability in actinide distribution between body organs in different subjects. In combination with appropriate modification of rate constants in the model of systemic metabolism, such data can provide information on the variability of effective dose between individuals under apparently similar exposure conditions.

As indicated in Section 2 of this proposal, skeleton and liver concentration data from both Registries were combined to compare retention half-times and initial actinide concentrations in both organs. The data from both registries were very compatible for combined usage and data for other tissues and organs are expected to be equally compatible.

During exchange visits between personnel of the USTUR and DRMIA Registries, actinide concentration and residence time data will be exchanged and combined and applied toward regressions as indicated above.

The DRMIA has a number of cases on file who had liver impairments at the time of death, classified as "pathology group 3". The same concentration ratio techniques, described above, will be applied to tissue analytical results of this group to determine the influence of liver impairment on biokinetics of actinides in the body. Completion of this task is scheduled for June 1, 1998.

Task H

Analysis of urinary excretion has long been a primary tool for determination of body actinide content in workers of the nuclear industry. Also, the determination of relationships between actinide body content and urinary excretion has been a primary goal of both Registries since their inception (Kathren et al. 1987; Kathren and McInroy 1991; Suslova 1995). The estimation of body actinide content from urinary excretion data is also the subject of a number of metabolic models, which have eventually evolved into those developed for ICRP 67 (1994) and those proposed by Khokhryakov et al. (1994). Combination of the urinalysis data and tissue analytical data of both Registries may result in verification or modification of those models. It could also elucidate factors that might influence the body content-excretion relationship such as dose dependence and temporal factors.

The DRMIA and the USTUR together have determined post mortem tissue content of actinides in more than 1000 individual cases. At least some actinide radiourinalysis data are available for most of these cases. The number of urinalyses per case is quite variable and dependent to a considerable degree on the type and magnitude of the exposure. Available tissue data differs from case to case; for example, the amount and specific portions of the skeleton differ from case to case. The combination of Registries data will provide greater numbers of comparable cases and additional stratification of data, thereby facilitating more reliable evaluation of the relationship between systemic contents of actinides and urinary excretion. An increase in the precision and accuracy of dosimetric estimates is expected because of the resultant increase in the number of subjects studied.

The question of the liver impairment influence on the systemic content-urinary excretion relationship will be investigated as part of this task. This task will be accomplished during exchange visits between personnel of the USTUR and the DRMIA and the anticipated completion date is June 1, 1999.

Task I

DRMIA investigations have shown that the ^{241}Am content of the body, measured by in vivo counting, correlates well with the ^{239}Pu body burden estimates based on urinalyses and analysis of tissues collected at autopsy. The DRMIA currently has whole body counters based on NaI(Tl) detectors which are used primarily for screening of workers with relatively high body burdens of plutonium. It is their intent to upgrade the facility by replacement of the NaI(Tl) detectors with phoswich detectors. This would enhance the sensitivity of the facility so that it can be used for characterization of intake and retention of actinide elements.

The first phase of this task consists of calibration of the equipment as it now exists for verification of data already collected and it will be accomplished during the first year of this proposed work. During the second year of the project, new detectors will be purchased and installed with initial calibration. During the final year, refined estimates of detector efficiency will be made and the results of whole body counts of Mayak workers will be compared to urinalysis data of the same subjects. Detector calibration can be accomplished with use of a phantom library maintained by Pacific Northwest National Laboratories (PNNL) at Richland, Washington. The phantom library includes the USTUR-owned ^{241}Am phantoms which are on long-term loan to PNNL, the administrator of their loan and usage by other laboratories. These phantoms are of particular applicability to the DRMIA program.

Task J

During the years of DRMIA operation a number of documents regarding plutonium metabolism were produced and classified for reasons of security. These have been recently declassified and contain a wealth of important scientific information worthy of sharing with the world scientific community. DRMIA and USTUR scientists will jointly undertake scientific review, verification, and translation of these documents into English and preparation of manuscripts for submission to peer-reviewed scientific journals for publication. For those documents for which publication in the peer-reviewed scientific literature is not warrented, open literature publication and access will be obtained via the existing topical report publication of the USTUR, which includes assignment of a number and availability through the Office of Scientific and Technical Information (OSTI).

During the first year of the proposed project, papers will be prepared and submitted for publication on the following three topics: (a) solubility

classification of workplace aerosols, (b) metabolism of plutonium and americium in occupationally-exposed people, and (c) a model describing plutonium clearance from the lung. During the second year additional papers dealing with solubility classification of aerosols, potential modification of lung clearance models, and actinide metabolism in the general Russian population will be prepared. Papers dealing with actinide metabolism and dosimetry are planned for the final year of the proposed project. The goal is publication of three papers annually.

Task K

The feasibility of using autoradiographic methods on DRMIA samples depends on a number of factors including availability of lung, lymph node, and liver samples at autopsy. Since autoradiography of tissue samples is not a particularly sensitive detection technique, it is necessary that tissues used are from cases with sufficiently high plutonium body burdens. DRMIA cases of the past have had such burdens; however, there are expected to be fewer such cases coming to autopsy in the future. Paraffin blocks of tissues from previous USTUR and DRMIA cases are another possibility.

There are two possible means of accomplishing this task and both will be explored. They are:

1. Transportation of the samples to USTUR laboratories for autoradiographic processing. This would require cooperation of both U. S. and Russian customs and there might be additional requirements of the Washington State University Institutional Review Board regarding Human Subjects Review of the USTUR.

2. Development of autoradiographic capability within the DRMIA laboratories at Ozersk. This would require procurement of reagents and training of personnel. Although DRMIA personnel have little experience with autoradiography, two USTUR staff members have extensive experience in this field, R. E. Filipy and G. E. Dagle (see curricula vitae in Appendix A).

Task L

Fluorescence in-situ hybridization (FISH) and glycophorin A (GLA) assays in Project 2.1 would be used to evaluate chromosomal translocations in peripheral lymphocytes and abnormal variants of glycophorin A in red blood cells and to compare these results with conventional dosimetry, bioassay evaluations, and exposure history. The primary goal of this task is to

correlate cytogenetic results with exposure and to establish a low-level dose-response curve which can be used as a biological dosimeter and possibly applied to predictions of biological effects. These assays require fresh blood samples from workers with sufficient body burdens of actinides to elicit chromosomal translocations. For the highest quality quantitative results, it will be necessary to transfer samples to U. S. laboratories in refrigerated containers.

There are two USTUR staff members that are involved in development of the bioassay analyses for use with USTUR cases, J. J. Russell and Shiping Bao (see curricula vitae in Appendix A).

If the logistics of collection and shipment of the samples for autoradiography and biomarker analyses can be worked out and their routine use on a sufficiently large number of samples can be demonstrated, they will be the subject of a proposal for additional funds.

DRMIA and USTUR investigators have been routinely communicating by e-mail and much can be accomplished by this means. During the August, 1995 visit of DRMIA scientists at the facilities of the USTUR, it became apparent that personal oral communication is far more effective than e-mail when major tasks are to be accomplished. For that reason, several interlaboratory visits are planned to accomplish the tasks outlined above. The planned visits are each 2-3 weeks in duration and are listed below with the tasks to be studied and/or completed with each visit.

Year 1

A. Two USTUR scientists to visit DRMIA facilities, in November or December, 1996. Tasks A, B, D, E, I, J, K, L, and the February 1, 1997 progress report will be addressed.

B. Three DRMIA scientists to visit USTUR facilities, April or May, 1997. Tasks A, B, C, D, E, K, L, and the June 1 progress report will be addressed during this visit.

Year 2

A. Three DRMIA scientists to visit USTUR facilities, December, 1997. Tasks D, E, F, G, H, I, J, and the February 1, 1998 progress report will be addressed.

A. Two USTUR scientists to visit DRMIA facilities, May, 1998. Tasks D, E, F, G, H, I, J, and the June 1 progress report will be addressed.

Year 3

A. Three DRMIA scientists to visit USTUR facilities, October, 1989. Tasks D, E, H, I, J, and the February 1, 1999 progress report will be addressed.

B. Two USTUR scientists to visit DRMIA facilities, June, 1999. The project final report will be prepared during this visit.

Assuming that the proposed project begins on October 1, 1996, progress reports are planned for February 1 and June 1 of each year. The third report of the year will consist of an annual report that contains a summary of the first two progress reports and a report of progress that occurred during the last four months of each project year. A final report containing all results of the proposed work will be issued on September 30, 1999.

5. QUALITY ASSURANCE/QUALITY CONTROL

There are two main concerns in the area of quality assurance/quality control; these are: (1) potential transcription errors when transferring data from hard copies of analytical results to computerized data basis and (2) the comparability of the radiochemical analytical data generated by the USTUR and the DRMIA. Each Registry will perform sufficient checks on data transcriptions to ensure the quality of its computerized data. Transcription of data to a common database will be accomplished electronically by the use of text files which will preclude the possibility of transcription errors. The DRMIA uses a database based on the software, FOXPRO, while the USTUR database is based on the software, PARADOX. Both are capable of importing and exporting files.

Comparability of radiochemical analytical data will be assessed by a series of performance tests on each laboratory. The performance tests, to be considered for use during an extended research program, will involve two levels of analytical capability:

a. determination of alpha radioactivity in acid solutions of ashed soft tissue and bone to provide a check on actinide separation technique and the electroplating process, and,

b. analysis of available Standard Reference Materials (SRM)--human tissue--prepared by the U. S. National Institute of

Standards and Technology (NIST) to provide checks on the complete radiochemical process, including ashing techniques as well as separations, electroplating, and alpha spectroscopy.

6. COLLABORATORS AND COLLABORATING INSTITUTIONS

The DRMIA was established by the Internal Dosimetry Laboratory of the First Branch of the Biophysics Institute (BIB), Ozersk, Russian Federation in the early 1970's. The Registry maintains databases containing exposure data, bioassay data, medical data, and radiochemical analytical data from post-mortem tissue samples of workers at the Mayak plutonium production facility at Ozersk, Russian Federation.

The USTUR originated in 1968 as the United States Transuranium Registry and it is presently operated under a U.S. Department of Energy grant to Washington State University (WSU) with headquarters at the Tri-Cities branch campus in Richland, WA, USA. The USTUR also maintains a database containing exposure data, bioassay data, medical data and radiochemical analytical data from post-mortem tissue samples; however, USTUR registrants have worked at many different nuclear facilities in the United States.

The DRMIA and the USTUR were formed with different approaches but with similar objectives. Both programs involve performance of autopsies on humans who were occupationally exposed to actinide elements and radiochemical analysis of the tissues collected at autopsy. Both programs have essentially the same primary objective which is to ensure adequacy of radiation protection standards for actinide elements, verifying or modifying, as appropriate, the existing biokinetic and dosimetric models on which the standards for actinide elements are based. Thus, it appears that combined evaluation of the large and unique data sets of both Registries will lead to improvement of applied dosimetry methods and increased precision of radiation protection standards. There are many similarities and differences in the scope and operation of the two programs as detailed in the first progress report of this project.

Project Research Teams consisting of principal scientists from each Registry are listed below:

United States	Russian Federation
Ronald E. Filipy (PI)[a]	Valentin F. Khokhryakov
Ronald L. Kathren (PI)	Klara Suslova
Royston H. Filby	Sergei A. Romanov

Dorothy Stuitt	Vladimir I. Chernikov
Sam Glover	Elena E. Aladova
Gerald Dagle	Tamara I. Kudryavtseva

[a]PI - Principal Investigator of the project research team.

Dr. Ruth Neta, U. S. Department of Energy (DOE) headquarters, will be the primary liaison betwen the DOE Office of International Health Studies and the DRMIA and USTUR principal investigators.

Personnel involvement--USTUR (Curricula vitae are in Appendix A)

Ronald E. Filipy, professor, will serve as the American project leader for Project 2.1 with oversight of all tasks. He will also be a direct participant at a technical level in tasks involving actinide biokinetics and internal dose assessment in the human body (tasks B, C, E, F, G, H, and I). His role in these tasks will include selection of Registries data needed for each task; supervision of data organization, manipulation, and analysis; interpretation of the analytical results; and preparation of written reports associated with the program. He will be the primary USTUR researcher involved in Task J, assisting the Russian scientists in translation and publication of previously classified Russian technical reports in English. Dr. Filipy has been on the staff of the USTUR for nearly six years and his activities during that time have included investigations of actinide biokinetics in tissues of occupationally-exposed workers of U. S. nuclear industries, the results of which have been published in peer-reviewed journals and presented at scientific meetings.

Royston H. Filby, professor with responsibility for the USTUR radiochemistry laboratories will be involved in an administrative and technical oversight role relating to tasks in which USTUR and DRMIA radiochemical analytical methods are compared (tasks A, D, and E). He will assist in planning the intercomparisons to be made, evaluation of the data, and in the interpretation of the results. Dr. Filby will serve as an internal reviewer for reports of radiochemical intercomparisons and quality assurance.

Dorothy Stuitt, radiochemist, will be the primary liaison between the DRMIA and the USTUR for radiochemistry (specifically tasks A and D). She will primarily be involved with intercomparisons of the radiochemical methods of the USTUR and the DRMIA. Ms. Stuitt joined the USTUR two years ago. She has more than 15 years of previous operational radioanalytical laboratory experience, including specific experience in analysis of bioassay and environmental samples for actinides.

Gerald E. Dagle, Associate Professor, will participate in the tissue autoradiography study (Task K). Prior to joining the WSU faculty, Dr. Dagle had extensive experience with autoradiography of biological samples during two decades at Pacific Northwest National Laboratories. He and Dr. R. E. Filipy are an established research team and they have published a number of studies utilizing autoradiographic techniques in peer-reviewed scientific literature and in technical reports.

Samuel L. Glover, radiochemist, will be involved in the intercomparison of DRMIA and USTUR radiochemical analytical methods (tasks A and D). His primary contribution to Project 2.1 will be the evaluation of workplace aerosols and the intercomparisons and calibration of in-vivo counting systems (tasks E and I). Prior to joining the USTUR two years ago, Mr. Glover was involved with in-vivo detection and bioassay procedures at other U. S. nuclear facilities.

Yong Ford, graduate research assistant with the USTUR, will assist in data management for all tasks of Project 2.1. She will assist investigators with the compilation, manipulation, and routine statistical analysis of data and with the preparation of data tables and figures for written reports. Ms. Ford has been involved in this kind of work with the USTUR for the past year.

The following USTUR staff members will participate in Tasks K and L, autoradiography and biomarker analyses, without direct charge to Project 2.1 as part of the normal USTUR research functions. Their curricula vitae are included in Appendix A.

Ronald L. Kathren, professor and director of the USTUR of which Project 2.1 is a part, will be involved in a project management and oversight capacity, and will be responsible for integration of Project 2.1 with the ongoing USTUR programs. He will be a direct participant at a technical level in tasks involving actinide biokinetics and internal dose assessment (tasks B, C, E, F, G, and H) by assisting in the planning stages, in data evaluation, and in the interpretation of the results. He will also serve as an internal reviewer of all written reports. Professor Kathren is a certified health physicist and has been involved with the USTUR since 1983. Since that time, he has published numerous peer-reviewed papers in scientific journals and made many presentations at scientific meetings regarding his investigations of actinide biokinetics and radiation dosimetry with Registries data.

Fluorescence in-situ hybridization and glycophorin A assays on suitable tissue samples (Task L) will be carried out by WSU faculty members John J. Russell and Shiping Bao. They are currently involved in the development of specific internal capabilities for those assays and, together with scientists at

Lawrence Livermore National Laboratory, are performing those assays on selected USTUR cases.

The overall objectives of the USTUR closely parallel those of Project 2.1; therefore, mechanisms for performance of many tasks of Project 2.1 are already in place. In addition to faculty and staff contributions discussed above, the USTUR and WSU will contribute a number of in-kind services to Project 2.1. These include the use of the fully computerized USTUR database; services of the computer network including e-mail, internet, and advanced calculational capabilities and programs; university library capabilities, specifically the health sciences related library of the College of Pharmacy. Participation in Project 2.1 of WSU/USTUR faculty members Dagle, Bao, Wilson and Russell will be supported directly by the primary USTUR grant or other sources and will not be charged to Project 2.1. Similarly, technical and additional administrative support will be directly supported primarily by the USTUR grant. The level of contribution to Project 2.1 directly supported by the primary USTUR grant will exceed one person-year. Assistance of College of Pharmacy and other W. S. U. faculty members are also available and can be utilized on an ad-hoc basis for this project. The WSU College of Pharmacy faculty includes scientists with established capabilities in areas related to the primary purpose of the project, including pharmacodynamics, heavy metal toxicology, and carcinogenesis. Specifically available to the project is Walter E. Wilson who holds academic appointments in both the College of Pharmacy and in Computer Sciences. Dr. Wilson has expertise in microdosimetry and track analysis and he will be involved in the interpretation of autoradiograms prepared as part of Task K.

Personnel involvement--DRMIA (Curricula vitae are in Appendix A)

Valentin F. Khokhryakov, chief of the laboratory of internal dosimetry, will serve as the Russian project leader for Project 2.1 with oversight of all tasks. He will also be a direct participant at a technical level in tasks involving actinide biokinetics and internal dose assessment in the human body (tasks B, E, F, G, H, and I) by assisting in the planning and by supervision of data analysis. He will also play a key role in interpretation of the results and report preparation. Dr. Khokhryakov has had a long and distinguished career in radiation dosimetry; it was largely through his efforts that the Laboratory for Internal Dosimetry was organized. He is the author of numerous Russian and English publications.

Klara G. Suslova, chemist and senior scientist, has been involved with the autopsy-tissue analysis program since it began. She will be the primary Russian liaison between the DRMIA and USTUR radiochemical analytical

groups and play a key role in the exchange of samples and intercomparisons of analytical results (task A) as well as in the coordination of autopsy sampling protocols and radiochemical analytical methods used by both Registries (tasks B, C and D). Dr Suslova will also be involved in tasks involving actinide biokinetics studies (tasks G and H) by compiling and reviewing the DRMIA data needed for those tasks.

Sergey A. Romanov, mathematician and group leader of the DRMIA data management group, will serve as the DRMIA data management and analysis expert, especially for those tasks involving large data sets (tasks F, G, and H). Mr. Romanov has a thorough knowledge of automated databases and good familiarity with the data collected by the DRMIA. He also has a good command of the English language which is useful in communications efforts between USTUR and DRMIA investigators.

Vladimir I. Chernikov, physicist and group leader of the in-vivo bioassay facility, will represent the DRMIA in calibration and intercomparison activities involving that facility (task I). He also has expertise with the detection instrumentation used by the radiochemistry laboratory and will be involved in the analytical intercomparison activities in that regard (task D).

Elena E. Aladova, chief of the radiochemistry group, will be involved in the laboratory analysis of samples used in the DRMIA-USTUR intercomparison activity (task D). She will also be the key figure in the physico-chemical characterization of workplace aerosols (task E) having been involved with development and use of the "dialysis" method in use by the Laboratory of Internal Dosimetry to determine in-vitro solubility of aerosols. Ms. Aladova also has a good command of the English language and will be instrumental in the translation of previously classified Russian documents into English.

Tamara I. Kudryavtseva, research scientists, will be involved in the coordination of tissue sampling methods (task C) by analyzing data from specific samples to be included in the autopsy protocol. She will be involved in the analysis of plutonium concentration data in the lungs, lymph nodes, and other body tissues and organs (tasks G and H).

7. HUMAN SUBJECTS REVIEW

The USTUR is reviewed annually by the Washington State University Institutional Review Board (IRB) to assure full legal and ethical compliance with respect to the use of human subjects for research purposes.

The DRMIA program is operated in full accordance with laws of the Russian Federation.

had extensive experience with autoradiography of biological samples during two decades at Pacific Northwest National Laboratories. He and Dr. R. E. Filipy are an established research team and they have published a number of studies utilizing autoradiographic techniques in peer-reviewed scientific literature and in technical reports.

Fluorescence in-situ hybridization and glycophorin A assays on suitable tissue samples (Task L) will be carried out by W. S. U. faculty members John J. Russell and Shiping Bao. They are currently involved in the development of specific internal capabilities for those assays and, together with scientists at Lawrence Livermore National Laboratory, are performing those assays on selected USTUR cases.

The overall objectives of the USTUR closely parallel those of Project 2.1; therefore, mechanisms for performance of many tasks of Project 2.1 are already in place. In addition to faculty and staff contributions discussed above, the USTUR and Washington State University will contribute a number of in-kind services to Project 2.1. These include the use of the fully computerized USTUR database; services of the computer network including e-mail, internet, and advanced calculational capabilities and programs; university library capabilities, specifically the health sciences related library of the College of Pharmacy. Assistance of College of Pharmacy and other W. S. U. faculty members are also available and can be utilized on an ad-hoc basis for this project. The W. S. U. College of Pharmacy faculty includes scientists with established capabilities in areas related to the primary purpose of the project, including pharmacodynamics, heavy metal toxicology, and carcinogenesis. Specifically available to the project is Walter E. Wilson who holds academic appointments in both the College of Pharmacy and in Computer Sciences. Dr. Wilson's expertise is in microdosimetry and track analysis and he will be involved in the interpretation of autoradiograms prepared as part of Task K.

Personnel involvement--DRMIA (Curricula vitae are in Appendix A)

Valentin F. Khokhryakov, chief of the laboratory of internal dosimetry, will serve as the Russian project leader for Project 2.1 with oversight of all tasks. He will also be a direct participant at a technical level in tasks involving actinide biokinetics and internal dose assessment in the human body (tasks B, E, F, G, H, and I) by assisting in the planning and by supervision of data analysis. He will also play a key role in interpretation of the results and report preparation. Dr. Khokhryakov has had a long and distinguished career in radiation dosimetry; it was largely through his efforts that the Laboratory for Internal Dosimetry was organized. He is the author of numerous Russian and English publications.

Klara G. Suslova, chemist and senior scientist, has been involved with the autopsy-tissue analysis program since it began. She will be the primary Russian liaison between the DRMIA and USTUR radiochemical analytical groups and play a key role in the exchange of samples and intercomparisons of analytical results (task A) as well as in the coordination of autopsy sampling protocols and radiochemical analytical methods used by both Registries (tasks B, C and D). Dr Suslova will also be involved in tasks involving actinide biokinetics studies (tasks G and H) by compiling and reviewing the DRMIA data needed for those tasks.

Sergey A. Romanov, mathematician and group leader of the DRMIA data management group, will serve as the DRMIA data management and analysis expert, especially for those tasks involving large data sets (tasks F, G, and H). Mr. Romanov has a thorough knowledge of automated databases and good familiarity with the data collected by the DRMIA. He also has a good command of the English language which is useful in communications efforts between USTUR and DRMIA investigators.

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Tamara I. Kudryavtseva, research scientists, will be involved in the coordination of tissue sampling methods (task C) by analyzing data from specific samples to be included in the autopsy protocol. She will be involved in the analysis of plutonium concentration data in the lungs, lymph nodes, and other body tissues and organs (tasks G and H).

7. HUMAN SUBJECTS REVIEW

8. REFERENCES

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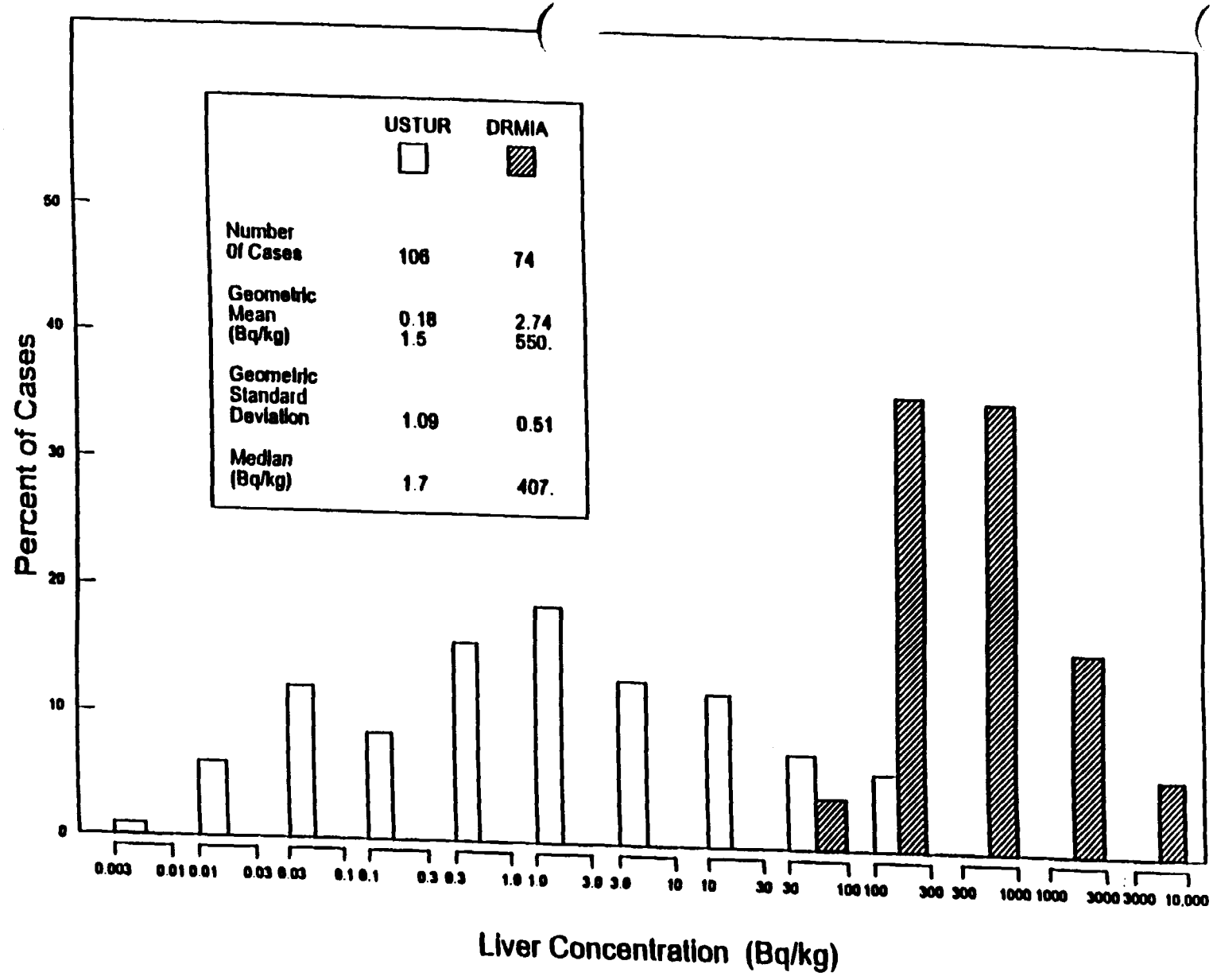

Figure 1. Frequency distribution of plutonium liver concentrations in USTUR and DRMIA cases.

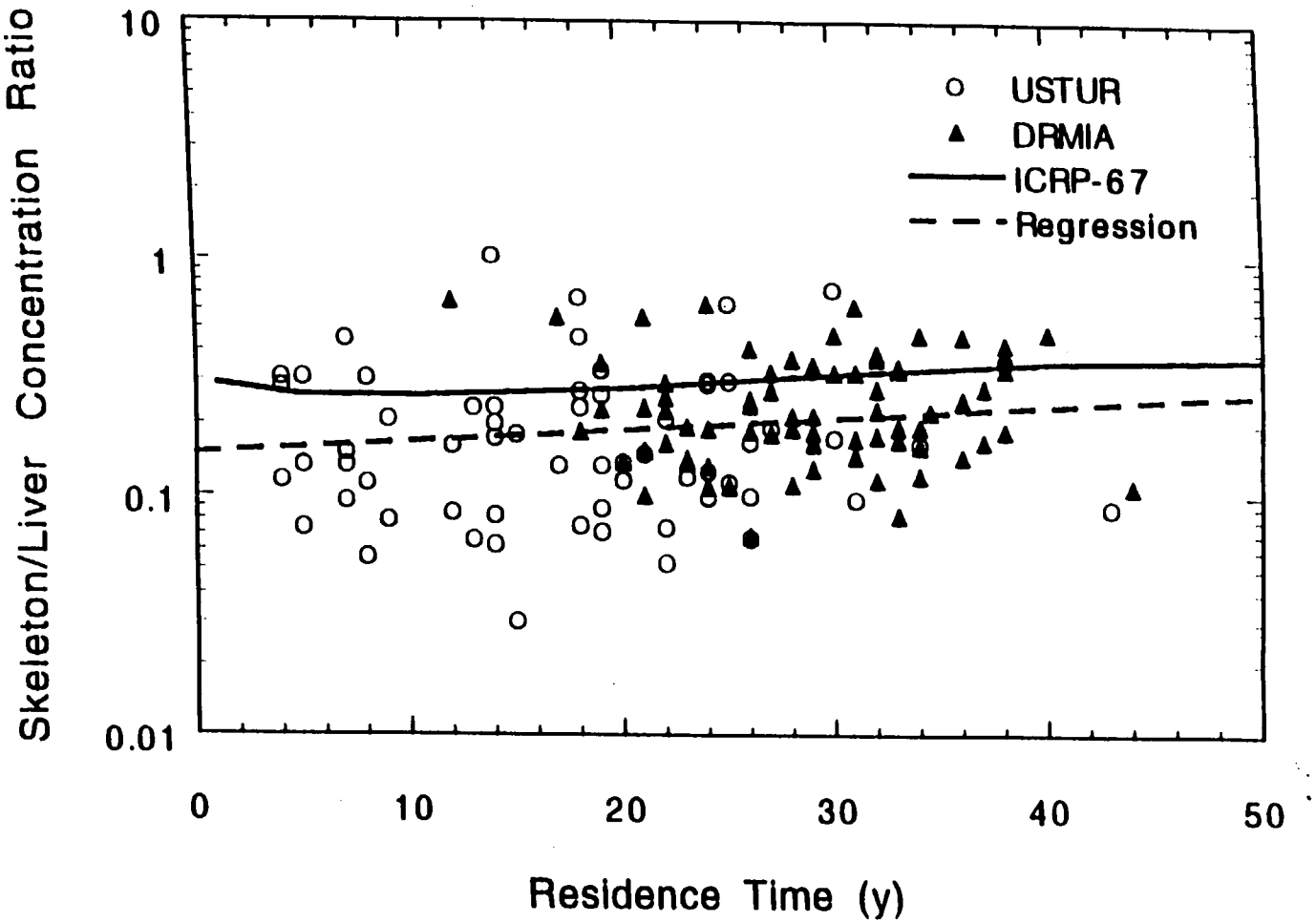

Figure 2. Skeleton: liver plutonium concentration ratios as a function of time between exposure and death (residence time) in USTUR and DRMIA cases, including the predicted ratios calculated by ICRP (1994) methodology and the regression line through the observed data.

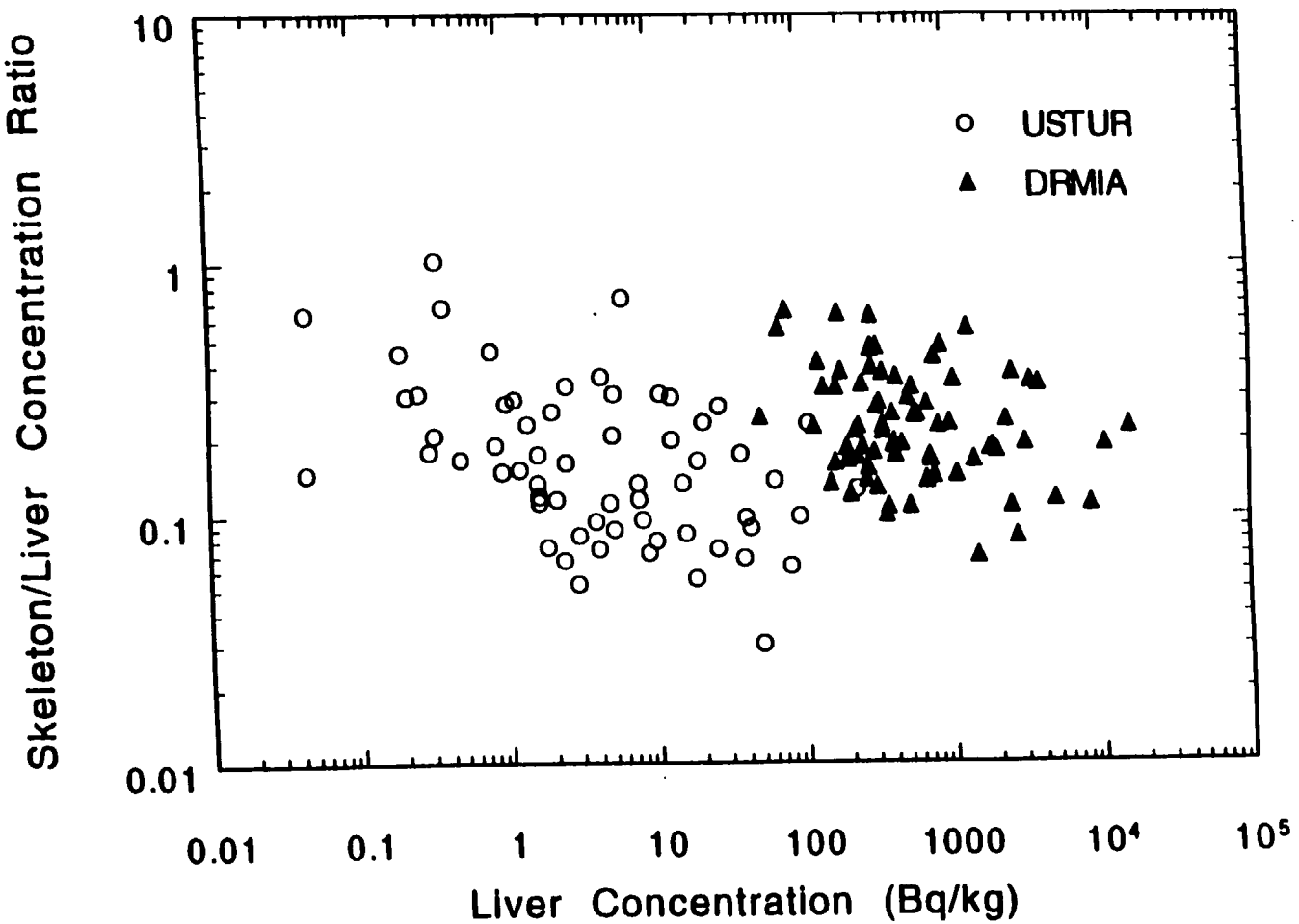

Figure 3. Skeleton: liver plutonium concentration ratios as a function of liver concentrations in USTUR and DRMIA cases.

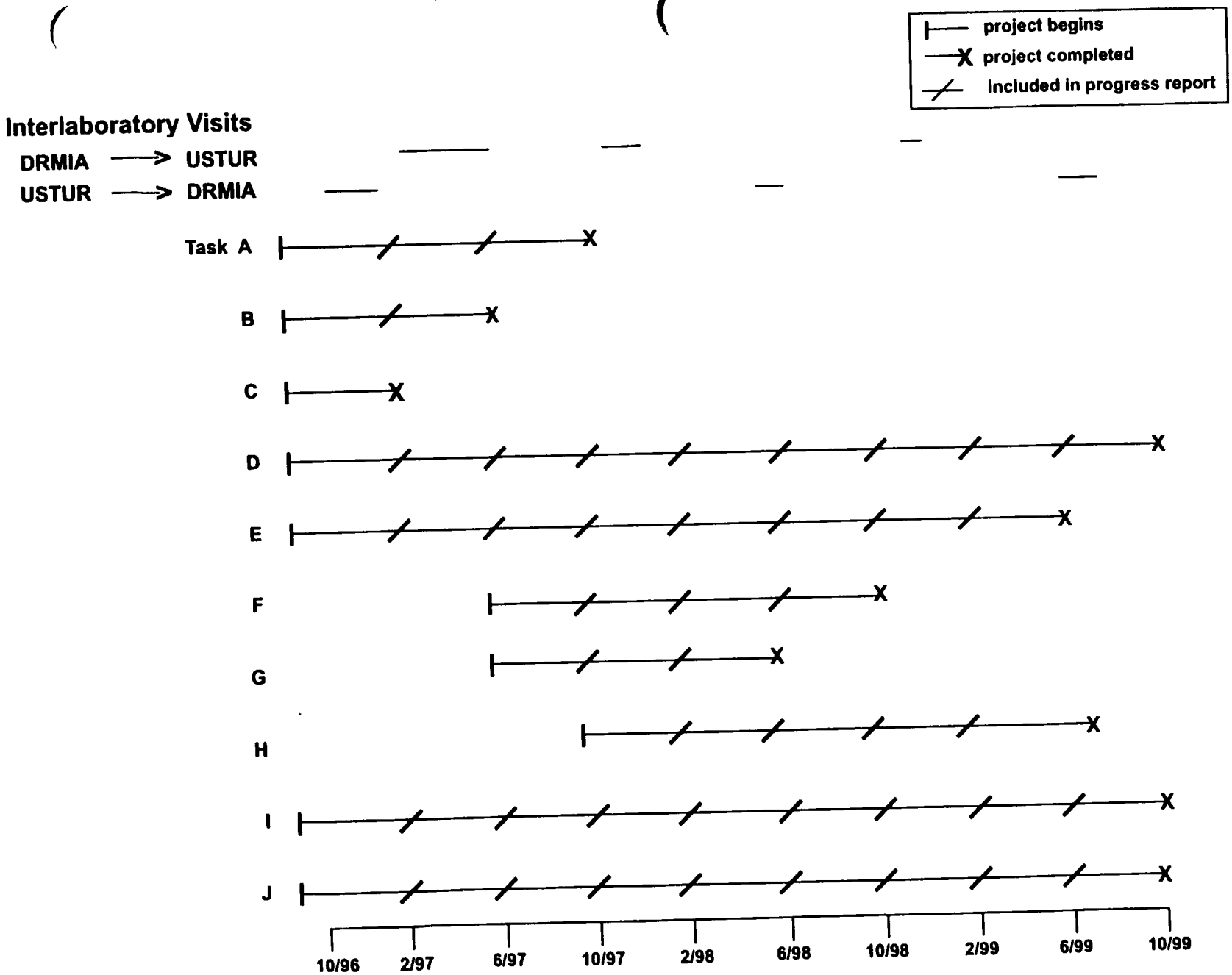

Figure 4. Schedule of proposed tasks.

Budget Request Format for EH-63 Funded Projects

Project/Subproject Title: Addendum to USTUR (Russian Proj)		**Period of Support:** 10/1/96-9/30/97	
Institution: Washington State University, College of Pharmacy, US Transuranium and Uranium Registries			
Complete Address: 100 Sprout Rd.			
Richland, WA 99352		509-372-7317	509-375-1817
		Telephone #:	**Fax #:**
Name of Principal Investigator: Ronald L. Kathren			
Name of Contact Person: Ronald E. Filipy			
Requested Items			
A. Equipment (itemize)			
Please list description of equipment			**Amount in U.S. $$**
			$$
			$$
			$$
			$$
Please justify equipment purchase on separate page(s)		**Subtotal>**	**$$** 0
B. Supplies (itemize)			**Amount in U.S. $$**
Translation Fee			**$$** 5,000
Publications, page			**$$** 6,000
Telephone, Fax Shipping			**$$** 2,000
			$$
Please justify supplies on separate page(s)		**Subtotal>**	**$$** 13,000
C. Estimated Travel Costs	**Destination**	**Travel Dates**	**Amount in U.S. $$**
Please list names of travellers			**$$**
2 scientists to Russia for two weeks			**$$** 10,000
Professional meeting			**$$** 2,000
			$$
			$$
Please report justification for travel on separate page(s)		**Subtotal>**	**$$** 12,000
D. Personnel and Other Costs. *see attached subcontracts			10,000
D. i) Project Personnel Costs	**Percent Effort**		**Amount in U.S. $$**
Please list names of staff members			**$$**
See attached list for personnel			**$$**
			$$
			$$
			$$
Please list duties of each staff on separate pages(s)		**Subtotal>**	**$$** 156,008
D.ii) Indirect and or other costs			**Amount in U.S. $$**
			$$
			$$
			$$
			$$
Please itemize these costs with explanations for each cost		**Subtotal>**	**$$** 81,949
		Total Costs	**$$** 272,957
E. Other Sources of Funding			
Project Title(s):			
Source of Funds:			
Percent effort of each project staff listed above See attached personnel list			

Budget Request Format for EH-63 Funded Projects

Project/Subproject Title: Addendum to USTUR (Russian Proj)		**Period of Support:** 10/1/97-9/30/98	
Institution: Washington State Univeristy, College of Pharmacy,		US Transuranium and Uranium Registries	
Complete Address: 100 Sprout Rd,			
Richland, WA 99352		509-372-7317	509-375-1817
		Telephone #:	**Fax #:**
Name of Principal Investigator: Ronald L. Kathren			
Name of Contact Person: Ronald E. Filipy			
Requested Items			
A. Equipment (itemize)			
Please list description of equipment			**Amount in U.S. $$**
			$$
			$$
			$$
			$$
Please justify equipment purchase on separate page(s)		**Subtotal>**	**$$** 0
B. Supplies (itemize)			**Amount in U.S. $$**
Translation Fee			**$$** 5,200
Publications, Page			**$$** 6,240
Telephone, Tax, Shipping			**$$** 2,088
			$$
Please justify supplies on separate page(s)		**Subtotal>**	**$$** 13,528
C. Estimated Travel Costs	**Destination**	**Travel Dates**	**Amount in U.S. $$**
Please list names of travellers			**$$**
2 scientist to Russia for two weeks			**$$** 10,400
Professional Meeting			**$$** 2,088
			$$
			$$
Please report justification for travel on separate page(s)		**Subtotal>**	**$$** 12,488
D. Personnel and Other Costs. *see attached - Subcontracts			10,400
D. i) Project Personnel Costs	**Percent Effort**		**Amount in U.S. $$**
Please list names of staff members			**$$**
See attached list of personnel			**$$**
			$$
			$$
			$$
Please list duties of each staff on separate pages(s)		**Subtotal>**	**$$** 162,304
D.ii) Indirect and or other costs			**Amount in U.S. $$**
			$$
			$$
			$$
			$$
Please itemize these costs with explanations for each cost		**Subtotal>**	**$$** 85,027
		Total Costs	**$$** 283,747
E. Other Sources of Funding			
Project Title(s):			
Source of Funds:			
Percent effort of each project staff listed above See attached personnel list.			

Budget Request Format for EH-63 Funded Projects

Project/Subproject Title: Addendum to USTUR (Russian Proj)		**Period of Support:** 10/1/98-9/30/99	
Institution: Washington State University, College of Pharmacy, US Transuranium and Uranium Registries.			
Complete Address: 100 Sprout Rd.			
Richland, WA 99352		509-372-7317	509-375-1817
		Telephone #:	**Fax #:**
Name of Principal Investigator: Ronald L. Kathren			
Name of Contact Person: Ronald E. Filipy			
Requested Items			
A. Equipment (itemize)			
Please list description of equipment			**Amount in U.S. $$**
			$$
			$$
			$$
			$$
Please justify equipment purchase on separate page(s)		**Subtotal>**	**$$** 0
B. Supplies (itemize)			**Amount in U.S. $$**
Translation Fee			**$$** 5,408
Publications, Page			**$$** 6,490
Telephone, Fax, Shipping			**$$** 2,172
			$$
Please justify supplies on separate page(s)		**Subtotal>**	**$$** 14,070
C. Estimated Travel Costs	**Destination**	**Travel Dates**	**Amount in U.S. $$**
Please list names of travellers			**$$**
2 scientist to Russian for Two weeks			**$$** 10,816
Professional meeting			**$$** 2,172
			$$
			$$
Please report justification for travel on separate page(s)		**Subtotal>**	**$$** 12,988
D. Personnel and Other Costs. *see attached - subcontracts			10,816
D. i) Project Personnel Costs	**Percent Effort**		**Amount in U.S. $$**
Please list names of staff members			**$$**
See attached list for personnel			**$$**
			$$
			$$
			$$
Please list duties of each staff on separate pages(s)		**Subtotal>**	**$$** 168,874
D.ii) Indirect and or other costs			**Amount in U.S. $$**
			$$
			$$
			$$
			$$
Please itemize these costs with explanations for each cost		**Subtotal>**	**$$** 86,581
		Total Costs	**$$** 293,329
E. Other Sources of Funding			
Project Title(s):			
Source of Funds:			
Percent effort of each project staff listed above See attached personnel list.			

Title: Addendum to USTUR (Russian Project)
iod: March 1, 1996 through February 28, 1999

	Title	FTE	Year One	Year Two	Year Three	Total
Personnel:						
Faculty						
Ron Filipy	Professor	80%	67,053	69,735	72,524	209,312
Gerald D. Dagle	Asssoc. Prof.	15%	9,948	10,346	10,760	31,054
Ron Filby	Professor	10%	11,710	12,178	12,665	36,553
Dorothy Stuit	Project Assoc.	15%	7,983	8,303	8,635	24,921
Sam Glover	Project Assoc.	10%	6,568	6,831	7,104	20,503
Total Faculty Personnel			103,262	107,393	111,688	322,343
Graduate Students						
Yong Ford	Res. Asst. I	50%	9,580	9,963	10,362	29,905
Total Graduate Personnel			9,580	9,963	10,362	29,905
Administrative Support						
June Markel		20%	5,623	6,073	6,559	18,255
Total Administrative Personnel			5,623	6,073	6,559	18,255
Total Personnel:			118,465	123,429	128,609	370,503
Wages:						
Yong Ford Summer Appt.			3,104	3,228	3,357	9,689
Total Wages:			3,104	3,228	3,357	9,689
ıefits:			34,439	35,647	36,908	106,994
Total Personnel & Benefits:			156,008	162,304	168,874	487,185
Supplies:						
Translation Fee			5,000	5,200	5,408	15,608
Publications, Page Charges			6,000	6,240	6,490	18,730
Telephone, FAX, Shipping			2,000	2,088	2,172	6,260
Total Supplies:			13,000	13,528	14,070	40,598
Travel:						
2 Scientists to Russia for two weeks			10,000	10,400	10,816	31,216
Professional Meeting			2,000	2,088	2,172	6,260
Total Travel:			12,000	12,488	12,988	37,476
Subcontracts:						
Battelle - In-vivo counting			10,000	10,400	10,816	31,216
Total Subcontracts:			10,000	10,400	10,816	31,216
Total Direct Costs:			191,008	198,720	206,748	596,476
Indirect Costs:			81,949	85,027	86,581	253,557
Total Project Cost			272,957	283,747	293,329	850,033